SEQUENCE LISTING

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<110> Aranya Manosroi
      Jiradej Manosroi
      Chatchai Tayapiwatana
      Friedrich Goetz
      Rolf-Guenther Werner
<120> Methods for Large Scale Production of Recombinant
      DNA-Derived tPA or K2S Molecules
<130> 0652.2190001
<150> 60/268,574
<151> 2001-02-15
<150> GB 0027779.8
<151> 2000-11-14
<160> 25
<170> PatentIn Ver. 2.1
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      sequence of N-terminal part of K2S protein
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                                                                   18
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<211> 1128
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      sequence for OmpA-K2S fusion protein
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gcggcctctg agggaaacag tgactgctac tttgggaatg ggtcagccta ccgtggcacg 120
cacagoctca cogagtoggg tgcctcctgc ctcccgtqqa attccatqat cctqataqqc 180
aaggtttaca cagcacagaa ccccagtgcc caggcactgg gcctgggcaa acataattac 240
tgccggaatc ctgatgggga tgccaagccc tggtgccacg tgctgaagaa ccgcaggctq 300
acgtgggagt actgtgatgt geceteetge tecacetgeg geetgagaea gtacageeag 360
cctcagtttc gcatcaaagg agggctcttc gccgacatcg cctcccaccc ctggcaggct 420
gccatctttg ccaagcacag gaggtcgccc ggagagcggt tcctgtgcgg gggcatactc 480
atcagetect getggattet etetgeegee eactgettee aggagaggtt teegeeceae 540
cacctgacgg tgatcttggg cagaacatac cgggtggtcc ctggcgagga ggagcagaaa 600
tttgaagtcg aaaaatacat tgtccataag gaattcgatg atgacactta cgacaatgac 660
attgcgctgc tgcagctgaa atcggattcg tcccgctgtg cccaggagag cagcgtggtc 720
cgcactgtgt gccttccccc ggcggacctg cagctgccgg actggacgga gtgtgagctc 780
teeggetaeg geaageatga ggeettgtet eetttetatt eggagegget gaaggagget 840
catgicagae tgtacceate cageegetge acateacaae atttacttaa cagaacagte 900
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accgacaaca tgctgtgtgc tggagacact cggagcggcg ggccccaggc aaacttgcac 960
 gacgcctgcc agggcgattc gggaggcccc ctggtgtgtc tgaacgatgg ccgcatgact 1020
 ttggtgggca tcatcagctg gggcctgggc tgtggacaga aggatgtccc gggtgtgtac 1080
acaaaggtta ccaactacct agactggatt cgtgacaaca tgcgaccg
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 <213> Escherichia coli
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<211> 1065
<212> DNA
<213> Artificial Sequence
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      sequence for K2S protein
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tacacagcac agaaccccag tgcccaggca ctgggcctgg gcaaacataa ttactgccgg 180
aateetgatg gggatgeeaa geeetggtge caegtgetga agaacegeag getgaegtgg 240
gagtactgtg atgtgccctc ctgctccacc tgcggcctga gacagtacag ccagcctcag 300
tttcgcatca aaggagggct cttcgccgac atcgcctccc acccctggca ggctgccatc 360
tttgccaagc acaggaggtc gcccggagag cggttcctgt gcgggggcat actcatcagc 420
tectgetgga ttetetetge egeceaetge ttecaggaga ggttteegee ecaceaectg 480
acggtgatct tgggcagaac ataccgggtg gtccctggcg aggaggagca gaaatttgaa 540
gtcgaaaaat acattgtcca taaggaattc gatgatgaca cttacgacaa tgacattgcg 600
ctgctgcagc tgaaatcgga ttcgtcccgc tgtgcccagg agagcagcgt ggtccgcact 660
gtgtgccttc ccccggcgga cctgcagctg ccggactgga cggagtgtga gctctccggc 720
tacggcaagc atgaggcett gteteettte tatteggage ggetgaagga ggeteatgte 780
agactgtacc catccagccg ctgcacatca caacatttac ttaacagaac agtcaccgac 840
aacatgctgt gtgctggaga cactcggagc ggcgggcccc aggcaaactt gcacgacgcc 900
tgccagggcg attcgggagg ccccctggtg tgtctgaacg atggccgcat gactttggtg 960
ggcatcatca gctggggcct gggctgtgga cagaaggatg tcccgggtgt gtacacaaag 1020
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<211> 1128
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      sequence for OmpA-K2S fusion protein
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cacageetea eegagteggg tgeeteetge eteeegtgga attecatgat eetgatagge 180
aaggtttaca cagcacagaa ccccagtgcc caggcactgg gcctgggcaa acataattac 240
tgccggaatc ctgatgggga tgccaagccc tggtgccacg tgctgaagaa ccgcaggctg 300
acgtgggagt actgtgatgt gecetectge tecacetgeg geetgagaca gtacagecag 360
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gccatctttg ccaagcacag gaggtcgccc ggagagcggt tcctgtgcgg gggcatactc 480
atcageteet getggattet etetgeegee caetgettee aggagaggtt teegeeceae 540
cacctgacgg tgatcttggg cagaacatac cgggtggtcc ctggcgagga ggagcagaaa 600
tttgaagtcg aaaaatacat tgtccataag gaattcgatg atgacactta cgacaatgac 660
attgcgctgc tgcagctgaa atcggattcg tcccgctgtg cccaggagag cagcgtggtc 720
cgcactgtgt gccttccccc ggcggacctg cagctgccgg actggacgga gtgtgagctc 780
tccggctacg gcaagcatga ggccttgtct cctttctatt cggagcggct gaaggaggct 840
catgtcagac tgtacccatc cagccgctgc acatcacaac atttacttaa cagaacagtc 900
accgacaaca tgctgtgtgc tggagacact cggagcggcg ggccccaggc aaacttgcac 960
gacgcctgcc agggcgattc gggaggcccc ctggtgtgtc tgaacgatgg ccgcatgact 1020
ttggtgggca tcatcagctg gggcctgggc tgtggacaga aggatgtccc gggtgtgtac 1080
acaaaggtta ccaactacct agactggatt cgtgacaaca tgcgaccg
<210> 6
<211> 66
<212> DNA
<213> Escherichia coli
<400> 6
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gcggcc
<210> 7
<211> 1065
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: coding
      sequence for K2S protein
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tacacagcac agaaccccag tgcccaggca ctgggcctgg gcaaacataa ttactgccgg 180
aatcctgatg gggatgccaa gccctggtgc cacgtgctga agaaccgcag gctgacgtgg 240
gagtactgtg atgtgccctc ctgctccacc tgcggcctga gacagtacag ccagcctcag 300
tttcgcatca aaggagggct cttcgccgac atcgcctccc acccctggca ggctgccatc 360
tttgccaagc acaggaggtc gcccggagag cggttcctgt gcgggggcat actcatcagc 420
teetgetgga ttetetetge egeceaetge tteeaggaga ggttteegee ceaecacetg 480
acggtgatct tgggcagaac ataccgggtg gtccctggcg aggaggagca gaaatttgaa 540
gtcgaaaaat acattgtcca taaggaattc gatgatgaca cttacgacaa tgacattgcg 600
ctgctgcagc tgaaatcgga ttcgtcccgc tgtgcccagg agagcagcgt ggtccgcact 660
gtgtgccttc ccccggcgga cctgcagctg ccggactgga cggagtgtga gctctccggc 720
tacggcaagc atgaggcctt gtctcctttc tattcggagc ggctgaagga ggctcatgtc 780
agactgtacc catcagccg ctgcacatca caacatttac ttaacagaac agtcaccgac 840
aacatgctgt gtgctggaga cactcggagc ggcgggcccc aggcaaactt gcacgacgcc 900
tgccagggcg attcgggagg ccccctggtg tgtctgaacg atggccgcat gactttggtg 960
ggcatcatca gctggggcct gggctgtgga cagaaggatg tcccgggtgt gtacacaaag 1020
gttaccaact acctagactg gattcgtgac aacatgcgac cgtga
                                                                  1065
<210> 8
<211> 377
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: OmpA-K2S
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fusion protein

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1		1 90	1111	5		ALG	116	ALA	10		ьец	Ala	GTÀ	15	Ala
Thr	Val	Ala	Gln 20	Ala	Ala	Ser	Glu	Gly 25		Ser	Asp	Cys	Tyr 30	Phe	Gly
Asn	Gly	Ser 35	Ala	Tyr	Arg	Gly	Thr 40	His	Ser	Leu	Thr	Glu 45	Ser	Gly	Ala
Ser	Cys 50	Leu	Pro	Trp	Asn	Ser 55	Met	Ile	Leu	Ile	Gly 60	Lys	Val	Tyr	Thr
Ala 65	Gln	Asn	Pro	Ser	Ala 70	Gln	Ala	Leu	Gly	Leu 75	Gly	Lys	His	Asn	Tyr 80
Cys	Arg	Asn	Pro	Asp 85	Gly	Asp	Ala	Lys	Pro 90	Trp	Cys	His	Val	Leu 95	Lys
Asn	Arg	Arg	Leu 100	Thr	Trp	Glu	Tyr	Cys 105	Asp	Val	Pro	Ser	Cys 110	Ser	Thr
Суѕ	Gly	Leu 115	Arg	Gln	Tyr	Ser	Gln 120	Pro	Gln	Phe	Arg	Ile 125	Lys	Gly	Gly
Leu	Phe 130	Ala	Asp	Ile	Ala	Ser 135	His	Pro	Trp	Gln	Ala 140	Ala	Ile	Phe	Ala
Lys 145	His	Arg	Arg	Ser	Pro 150	Gly	Glu	Arg	Phe	Leu 155	Cys	Gly	Gly	Ile	Leu 160
Ile	Ser	Ser	Cys	Trp 165	Ile	Leu	Ser	Ala	Ala 170	His	Cys	Phe	Gln	Glu 175	Arg
Phe	Pro	Pro	His 180	His	Leu	Thr	Val	Ile 185	Leu	Gly	Arg	Thr	Tyr 190	Arg	Val
Val	Pro	Gly 195	Glu	Glu	Glu	Gln	Lys 200	Phe	Glu	Val	Glu	Lys 205	Tyr	Ile	Val
His	Lys 210	Glu	Phe	Asp	Asp	Asp 215	Thr	Tyr	Asp	Asn	Asp 220	Ile	Ala	Leu	Leu
Gln 225	Leu	Lys	Ser	Asp	Ser 230	Ser	Arg	Cys	Ala	Gln 235	Glu	Ser	Ser	Val	Val 240
Arg	Thr	Val	Cys	Leu 245	Pro	Pro	Ala	Asp	Leu 250	Gln	Leu	Pro	Asp	Trp 255	Thr
Glu	Cys	Glu	Leu 260	Ser	Gly	Tyr	Gly	Lys 265	His	Glu	Ala	Leu	Ser 270	Pro	Phe
Tyr	Ser	Glu 275	Arg	Leu	Lys	Glu	Ala 280	His	Val	Arg	Leu	Tyr 285	Pro	Ser	Ser
Arg	Cys 290	Thr	Ser	Gln	His	Leu 295	Leu	Asn	Arg	Thr	Val 300	Thr	Asp	Asn	Met
Leu 305	Cys	Ala	Gly	Asp	Thr 310	Arg	Ser	Gly	Gly	Pro 315	Gln	Ala	Asn	Leu	His 320

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Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp
Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly
            340
Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp
Trp Ile Arg Asp Asn Met Arg Pro Gly
    370
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<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: peptide
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Ser Glu Gly Asn
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<211> 6
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<223> Description of Artificial Sequence: peptide
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Ser Glu Gly Asn Ser Asp
<210> 11
<211> 354
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<223> Description of Artificial Sequence: K2S 174-527
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Gly Thr His Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn
Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala
Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly
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Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro 120 Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly 230 Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys 245 250 Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His 260 Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly 330 Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met 340 345

Arg Pro

<210> 12

<211> 331

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: K2S 197-527

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Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys 20 25 30

His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys Pro Trp Cys His

Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys Asp Val Pro Ser 50 60

Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile 65 70 75 80

Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala 85 90 95

Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys Gly 100 105 110

Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys Phe 115 120 125

Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg Thr 130 135 140

Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe Glu Val Glu Lys 145 150 155 160

Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp Ile 165 170 175

Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu Ser 180 185 190

Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu Pro 195 200 205

Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala Leu 210 215 220

Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu Tyr 225 230 235 240

Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val Thr 245 250 255

Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln Ala 260 265

Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Cys 275 280 285

Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly Leu 290 295 300

Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr Asn

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<210> 13

<211> 339

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: K2S 193-527,
 modified

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Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser 20 25 30

Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp 35 40 45

Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr 50 60

Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln 65 70 75 80

Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile 85 90 95

Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser 100 105 110

Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp 115 120 125

Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His 130 135 140

Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu 145 150 155 160

Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp 165 170 175

Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp

Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu 195 200 205

Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser 210 215 220

Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu 225 230 235 240

Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln

				245					250					255	
His	Leu	Leu	Asn 260	Arg	Thr	Val	Thr	Asp 265	Asn	Met	Leu	Cys	Ala 270	Gly	Asp
Thr	Arg	Ser 275	Gly	Gly	Pro	Gln	Ala 280	Asn	Leu	His	Asp	Ala 285	Cys	Gln	Gly
Asp	Ser 290	Gly	Gly	Pro	Leu	Val 295	Cys	Leu	Asn	Asp	Gly 300	Arg	Met	Thr	Leu
Val 305	Gly	Ile	Ile	Ser	Trp 310	Gly	Leu	Gly	Cys	Gly 315	Gln	Lys	Asp	Val	Pro 320
Gly	Val	Tyr	Thr	Lys 325	Val	Thr	Asn	Tyr	Leu 330	Asp	Trp	Ile	Arg	Asp 335	Asn
Met	Arg	Pro													
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<220 <220	3> De	escri odifi		on of	f Art	cific	cial	Sequ	ience	e: K2	2s 19	93-52	27,		
	0> 14 Leu		Glu	Ser 5	Gly	Ala	Ser	Суѕ	Leu 10	Pro	Trp	Asn	Ser	Met 15	Ile
Leu	Ile	Gly	Lys 20	Val	Tyr	Thr	Ala	Gln 25	Asn	Pro	Ser	Ala	Gln 30	Ala	Leu
Gly	Leu	Gly 35	Lys	His	Asn	Tyr	Cys 40	Arg	Asn	Pro	Asp	Gly 45	Asp	Ala	Lys
Pro	Trp 50	Cys	His	Val	Leu	Lys 55	Asn	Arg	Arg	Leu	Thr 60	Trp	Glu	Tyr	Суз
Asp 65	Val	Pro	Ser	Ser		Thr	Cys	Gly	Leu	Arg	Gln	Tyr	Ser	Gln	Dro
					70					75					
Gln	Phe	Arg	Ile	Lys 85		Gly	Leu	Phe		75	Ile	Ala	Ser	His 95	80
	Phe Gln	_		85	Gly	_			Ala 90	75 Asp				95	80 Pro
Trp		Ala	Ala 100	85 Ile	Gly Phe	Ala	Lys	His 105	Ala 90 Arg	75 Asp Arg	Ser	Pro	Gly 110	95 Glu	80 Pro Arg
Trp Phe	Gln	Ala Cys 115	Ala 100 Gly	85 Ile Gly	Gly Phe Ile	Ala	Lys Ile 120	His 105 Ser	Ala 90 Arg Ser	75 Asp Arg Cys	Ser Trp	Pro Ile 125	Gly 110 Leu	95 Glu Ser	80 Pro Arg Ala

Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr

Gln Asn Pro Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Asg Asg Pro Asg Gly Asg Ala Lys Pro Trp Cys His Val Leu Lys Asg Arg Arg Leu Thr Trp Glu Tyr Cys Asg Val Pro Trp Cys Ris Ser Thr Cys 80
Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu 85

Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys

<400> 16

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Ser	Ser 130	Cys	Trp	Ile	Leu	Ser 135	Ala	Ala	His	Cys	Phe 140	Gln	Glu	Arg	Phe
Pro 145	Pro	His	His	Leu	Thr 150	Val	Ile	Leu	Gly	Arg 155	Thr	Tyr	Arg	Val	Val
Pro	Gly	Glu	Glu	Glu 165	Gln	Lys	Phe	Glu	Val 170	Glu	Lys	Tyr	Ile	Val 175	His
Lys	Glu	Phe	Asp 180	Asp	Asp	Thr	Tyr	Asp 185	Asn	Asp	Ile	Ala	Leu 190	Leu	Gln
Leu	Lys	Ser 195	Asp	Ser	Ser	Arg	Cys 200	Ala	Gln	Glu	Ser	Ser 205	Val	Val	Arg
Thr	Val 210	Cys	Leu	Pro	Pro	Ala 215	Asp	Leu	Gln	Leu	Pro 220	Asp	Trp	Thr	Glu
Cys 225	Glu	Leu	Ser	Gly	Tyr 230	Gly	Lys	His	Glu	Ala 235	Leu	Ser	Pro	Phe	Туг 240
Ser	Glu	Arg	Leu	Lys 245	Glu	Ala	His	Val	Arg 250	Leu	Tyr	Pro	Ser	Ser 255	Arg
Суз	Thr	Ser	Gln 260	His	Leu	Leu	Asn	Arg 265	Thr	Val	Thr	Asp	Asn 270	Met	Leu
Cys	Ala	Gly 275	Asp	Thr	Arg	Ser	Gly 280	Gly	Pro	Gln	Ala	Asn 285	Leu	His	Asp
Ala	Cys 290	Gln	Gly	Asp	Ser	Gly 295	Gly	Pro	Leu	Val	Cys 300	Leu	Asn	Asp	Gly
Arg 305	Met	Thr	Leu	Val	Gly 310	Ile	Ile	Ser	Trp	Gly 315	Leu	Gly	Суз	Gly	Glr 320
Lys	Asp	Val	Pro	Gly 325	Val	Tyr	Thr	Lys	Val 330	Thr	Asn	Tyr	Leu	Asp 335	Trp
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	<220> <223> Description of Artificial Sequence: K2S 191-527, modified														

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Cys Leu Pro Trp Asn Ser Met Ile Leu Ile Gly Lys Val Tyr Thr Ala

Gln	Asn	Pro 35	Ser	Ala	Gln	Ala	Leu 40	Gly	Leu	Gly	Lys	His 45	Asn	Tyr	Суз
Arg	Asn 50	Pro	Asp	Gly	Asp	Ala 55	Lys	Pro	Trp	Cys	His 60	Val	Leu	Lys	Asn
Arg 65	Arg	Leu	Thr	Trp	Glu 70	Tyr	Суѕ	Asp	Val	Pro 75	Ser	Ser	Ser	Thr	Cys 80
Gly	Leu	Arg	Gln	Tyr 85	Ser	Gln	Pro	Gln	Phe 90	Arg	Ile	Lys	Gly	Gly 95	Leu
Phe	Ala	Asp	Ile 100	Ala	Ser	His	Pro	Trp 105	Gln	Ala	Ala	Ile	Phe 110	Ala	Lys
His	Arg	Arg 115	Ser	Pro	Gly	Glu	Arg 120	Phe	Leu	Суѕ	Gly	Gly 125	Ile	Leu	Ile
Ser	Ser 130	Cys	Trp	Ile	Leu	Ser 135	Ala	Ala	His	Cys	Phe 140	Gln	Glu	Arg	Phe
Pro 145	Pro	His	His	Leu	Thr 150	Val	Ile	Leu	Gly	Arg 155	Thr	Tyr	Arg	Val	Val 160
Pro	Gly	Glu	Glu	Glu 165	Gln	Lys	Phe	Glu	Val 170	Glu	Lys	Tyr	Ile	Val 175	His
Lys	Glu	Phe	Asp 180	Asp	Asp	Thr	Tyr	Asp 185	Asn	Asp	Ile	Ala	Leu 190	Leu	Gln
Leu	Lys	Ser 195	Asp	Ser	Ser	Arg	Cys 200	Ala	Gln	Glu	Ser	Ser 205	Val	Val	Arg
Thr	Val 210	Cys	Leu	Pro	Pro	Ala 215	Asp	Leu	Gln	Leu	Pro 220	Asp	Trp	Thr	Glu
Cys 225	Glu	Leu	Ser	Gly	Tyr 230	Gly	Lys	His	Glu	Ala 235	Leu	Ser	Pro	Phe	Tyr 240
Ser	Glu	Arg	Leu	Lys 245	Glu	Ala	His	Val	Arg 250	Leu	Tyr	Pro	Ser	Ser 255	Arg
Cys	Thr	Ser	Gln 260	His	Leu	Leu	Asn	Arg 265	Thr	Val	Thr	Asp	Asn 270	Met	Leu
Cys	Ala	Gly 275	Asp	Thr	Arg	Ser	Gly 280	Gly	Pro	Gln	Ala	Asn 285	Leu	His	Asp
Ala	Cys 290	Gln	Gly	Asp	Ser	Gly 295	Gly	Pro	Leu	Val	Cys 300	Leu	Asn	Asp	Gly
Arg 305	Met	Thr	Leu	Val	Gly 310	Ile	Ile	Ser	Trp	Gly 315	Leu	Gly	Cys	Gly	Gln 320
Lys	Asp	Val	Pro	Gly 325	Val	Tyr	Thr	Lys	Val 330	Thr	Asn	Tyr	Leu	Asp 335	Trp
Ile	Arg	Asp	Asn 340	Met	Arg	Pro									

<210> 17

<211> 308

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: K2S 220-527

<400> 17

Ser Ala Gln Ala Leu Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro $1 \\ 5 \\ 10 \\ 15$

Asp Gly Asp Ala Lys Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu 20 25 30

Thr Trp Glu Tyr Cys Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg 35 40 45

Gln Tyr Ser Gln Pro Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp 50 55

Ile Ala Ser His Pro Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg 65 70 75 80

Ser Pro Gly Glu Arg Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys
85 90 95

Trp Ile Leu Ser Ala Ala His Cys Phe Gln Glu Arg Phe Pro Pro His 100 105 110

His Leu Thr Val Ile Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu 115 120 125

Glu Glu Gln Lys Phe Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe 130 140

Asp Asp Asp Thr Tyr Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser 145 150 155 160

Asp Ser Ser Arg Cys Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys 165 170 175

Leu Pro Pro Ala Asp Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu 180 185 190

Ser Gly Tyr Gly Lys His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg 195 200 205

Leu Lys Glu Ala His Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser 210 215 220

Gln His Leu Leu Asn Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly 225 230 235 240

Asp Thr Arg Ser Gly Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln \$245\$ \$250\$

Gly Asp Ser Gly Gly Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr 260 270

Leu Val Gly Ile Ile Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val 275 280 285

Pro Gly Val Tyr Thr Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp 290 295 300

Asn Met Arg Pro

<210> 18

<211> 268

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: K2S 260-527

<400> 18

Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro Gln Phe Arg
1 10 15

Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro Trp Gln Ala 20 25 30

Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg Phe Leu Cys $35 \hspace{1cm} 40 \hspace{1cm} 45$

Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala Ala His Cys 50 60

Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile Leu Gly Arg 65 70 75 80

Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Glu Lys Phe Glu Val Glu 85 90 95

Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr Asp Asn Asp 100 105 110

Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys Ala Gln Glu 115 120 125

Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp Leu Gln Leu 130 135 140

Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys His Glu Ala 145 150 155

Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His Val Arg Leu 165 170 175

Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn Arg Thr Val $180 \,$ $185 \,$ $190 \,$

Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly Gly Pro Gln 195 200

Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly Pro Leu Val 210 215 220

Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile Ser Trp Gly 225 230 235

Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr Lys Val Thr

Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro 260 265

<210> 19

<211> 527

<212> PRT

<213> Homo sapiens

<400> 19

Ser Tyr Gln Val Ile Cys Arg Asp Glu Lys Thr Gln Met Ile Tyr Gln 1 5 10 15

Gln His Gln Ser Trp Leu Arg Pro Val Leu Arg Ser Asn Arg Val Glu 20 25 30

Tyr Cys Trp Cys Asn Ser Gly Arg Ala Gln Cys His Ser Val Pro Val 35 40

Lys Ser Cys Ser Glu Pro Arg Cys Phe Asn Gly Gly Thr Cys Gln Gln 50 55 60

Ala Leu Tyr Phe Ser Asp Phe Val Cys Gln Cys Pro Glu Gly Phe Ala 65 70 75 80

Gly Lys Cys Glu Ile Asp Thr Arg Ala Thr Cys Tyr Glu Asp Gln 85 90 95

Gly Ile Ser Tyr Arg Gly Thr Trp Ser Thr Ala Glu Ser Gly Ala Glu $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$

Cys Thr Asn Trp Asn Ser Ser Ala Leu Ala Gln Lys Pro Tyr Ser Gly 115 120 125

Arg Arg Pro Asp Ala Ile Arg Leu Gly Leu Gly Asn His Asn Tyr Cys 130 140

Arg Asn Pro Asp Arg Asp Ser Lys Pro Trp Cys Tyr Val Phe Lys Ala 145 150 155

Gly Lys Tyr Ser Ser Glu Phe Cys Ser Thr Pro Ala Cys Ser Glu Gly
165 170 175

Asn Ser Asp Cys Tyr Phe Gly Asn Gly Ser Ala Tyr Arg Gly Thr His

Ser Leu Thr Glu Ser Gly Ala Ser Cys Leu Pro Trp Asn Ser Met Ile 195 200 205

Leu Ile Gly Lys Val Tyr Thr Ala Gln Asn Pro Ser Ala Gln Ala Leu 210 215 220

Gly Leu Gly Lys His Asn Tyr Cys Arg Asn Pro Asp Gly Asp Ala Lys 225 230 235

Pro Trp Cys His Val Leu Lys Asn Arg Arg Leu Thr Trp Glu Tyr Cys 245 250 255

Asp Val Pro Ser Cys Ser Thr Cys Gly Leu Arg Gln Tyr Ser Gln Pro 260 265 270

 Gln Phe Arg Ile Lys Gly Gly Leu Phe Ala Asp Ile Ala Ser His Pro 275 280 285

Trp Gln Ala Ala Ile Phe Ala Lys His Arg Arg Ser Pro Gly Glu Arg 290 295 300

Phe Leu Cys Gly Gly Ile Leu Ile Ser Ser Cys Trp Ile Leu Ser Ala 305 310 315 320

Ala His Cys Phe Gln Glu Arg Phe Pro Pro His His Leu Thr Val Ile 325 330 335

Leu Gly Arg Thr Tyr Arg Val Val Pro Gly Glu Glu Glu Gln Lys Phe 340 345 350

Glu Val Glu Lys Tyr Ile Val His Lys Glu Phe Asp Asp Asp Thr Tyr 355 360 365

Asp Asn Asp Ile Ala Leu Leu Gln Leu Lys Ser Asp Ser Ser Arg Cys 370 375 380

Ala Gln Glu Ser Ser Val Val Arg Thr Val Cys Leu Pro Pro Ala Asp 385 390 395 400

Leu Gln Leu Pro Asp Trp Thr Glu Cys Glu Leu Ser Gly Tyr Gly Lys 405 410 415

His Glu Ala Leu Ser Pro Phe Tyr Ser Glu Arg Leu Lys Glu Ala His 420 425 430

Val Arg Leu Tyr Pro Ser Ser Arg Cys Thr Ser Gln His Leu Leu Asn $435 \hspace{1.5cm} 440 \hspace{1.5cm} 445$

Arg Thr Val Thr Asp Asn Met Leu Cys Ala Gly Asp Thr Arg Ser Gly 450 460

Gly Pro Gln Ala Asn Leu His Asp Ala Cys Gln Gly Asp Ser Gly Gly 465 470 475 480

Pro Leu Val Cys Leu Asn Asp Gly Arg Met Thr Leu Val Gly Ile Ile 485 490 495

Ser Trp Gly Leu Gly Cys Gly Gln Lys Asp Val Pro Gly Val Tyr Thr 500 505

Lys Val Thr Asn Tyr Leu Asp Trp Ile Arg Asp Asn Met Arg Pro $515 \\ 520 \\ 525$

<210> 20

<211> 12

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: coding
 sequence for SEGN

<400> 20

tctgagggaa ac

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<210> 21
<211> 22
<212> PRT
<213> Escherichia coli
<400> 21
Met Lys Lys Thr Ala Ile Ala Ile Ala Val Ala Leu Ala Gly Phe Ala
Thr Val Ala Gln Ala Ala
             20
<210> 22
<211> 42
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: primer
<400> 22
                                                                    42
gaggaggagg tggcccaggc ggcctctgag ggaaacagtg ac
<210> 23
<211> 42
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: primer
<400> 23
gaggaggagc tggccggcct ggcccggtcg catgttgtca cg
                                                                    42
<210> 24
<211> 26
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: primer
<400> 24
                                                                    26
acatgcgacc gtgacaggcc ggccag
<210> 25
<211> 26
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence: primer
<400> 25
ctggccggcc tgtcacggtc gcatgt
                                                                    26
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